II. REMARKS

A. Status of the Claims

Claims 9 and 27 were amended without prejudice. Support for the amendments to claim 9 can be found, e.g., in Examples 6 and 7 (page 62-67 of the specification). Support for the amendments to claim 27 can be found, e.g., on page 19, lines 3-9, of the specification.

Claims 1-8 and 10-22 were previously canceled without prejudice.

Claims 9 and 23-29 are pending.

Applicants respectfully submit that no new matter has been added by virtue of these amendments.

B. Claim Rejections- 35 U.S.C. § 112

In the Office Action, claims 9 and 23-29 were rejected under 35 U.S.C. § 112, second paragraph, allegedly "for omitting essential elements." See Office Action, page 2. The Examiner stated that "[t]he omitted elements are: complement, peripheral blood mononuclear cells, or an attached toxin that will produce cytotoxic activity against the cell lines HepG2 or Huh-7 when the monoclonal antibody against residues 375-580 of GPC3 is bound to them." See Office Action, page 2.

The rejection is respectfully traversed. However, to advance the prosecution of the application, claim 9 has been amended without prejudice to recite in part that an isolated monoclonial antibody has a cytotoxic activity "in the presence of complement or peripheral blood mononuclear cells."

Accordingly, withdrawal of the rejection is respectfully requested.

In the Office Action, claim 27 was rejected under 35 U.S.C. § 112, second paragraph, allegedly as indefinite for containing the term "derived." The Examiner stated that "[a]mendment of the claim to replace "derived" with "obtained" would obviate this rejection." See Office Action, page 3.

The rejection is respectfully traversed. However, to advance the prosecution of the application, claim 27 has been amended without prejudice in accordance with the Examiner's suggestion- the term "derived" has been replaced with the term "obtained."

Accordingly, withdrawal of the rejection is respectfully requested.

In the Office Action, claims 9 and 23-29 were rejected under 35 U.S.C. §112, first paragraph, on the grounds of enablement. However, the Examiner did acknowledge that the specification is enabled for "antibodies ch.M3C11 and ch.M1E07, wherein the antibody has ADCC activity or CDC activity *in vitro* against the cell line, HepG2 or HUH-7 in the presence of complement or peripheral blood mononuclear cells or when conjugated to a toxin or radioactive materials."

The rejection is respectfully traversed. However, to advance the prosecution of the application, claim 9 has been amended without prejudice to recite in part that an isolated monoclonal antibody "has a cytotoxic activity **in vitro** against the cell line **HepG2 in the presence of complement or peripheral blood mononuclear cells**." (emphasis added).

Applicants respectfully submit that the present specification enables one skilled in the art to practice the invention recited in the present claims without undue experimentation. Accordingly, Applicants submit that the present claims are enabled. See, e.g., *In re Wands*, 858 F2d. 731 (Fed. Cir. 1988).

For the foregoing reasons, withdrawal of the rejection is respectfully requested.

Claims 9 and 23-29 were rejected under 35 U.S.C. § 112, first paragraph, allegedly because the specification does not contain a written description for the feature "wherein the antibody has a cytotoxic activity against the cell line Huh-7" in claim 9. See Office Action, page 10.

The rejection is respectfully traversed. However, to advance the prosecution of the application, claim 9 has been amended without prejudice. Amended claim 9 does not recite the objected term.

Accordingly, withdrawal of the rejection is respectfully requested.

Claims 9 and 23-29 were rejected under 35 U.S.C. § 112, first paragraph, allegedly "as failing to comply with the written description requirement." See Office Action, page 10. The Examiner stated that "[t]he claims are broadly drawn to an isolated monoclonal antibody against a peptide consisting of amino acid residues 375-380 of GPC3 as set forth in SEQ ID No: 4, wherein the antibody has a cytotoxic activity against the cell line, HepG2 or HUH-7." See Office Action, page 11.

The rejection is respectfully traversed. However, to advance the prosecution of the application, claim 9 has been amended without prejudice.

Applicants submit that amended claim 9 is narrower in scope than claim 9 that was considered by the Examiner when interposing the rejection. In particular, claim 9 was amended without prejudice to recite the terms "in vitro" and "in the presence of complement or peripheral blood mononuclear cells." Moreover, amended claim 9 does not recite cell line HuH-7.

Specifically, amended claim 9 recites:

> An isolated monoclonal antibody against a peptide consisting of amino acid residues 375-580 of GPC 3 as set forth in SEQ ID NO: 4, wherein the antibody has a cytotoxic activity in vitro against the cell line HepG2 in the presence of complement or peripheral blood mononuclear cells."

Applicants submit that the Examples of the specification demonstrate that a plurality of antibodies (e.g., ch.M3C11 and ch.M1E07) exhibit the cytotoxic activity. In fact, it appears that the Examiner himself acknowledged this position with regard to the enablement rejection, when the Examiner stated that the specification is enabled for antibodies "ch.M3C11 and ch.M1E07, wherein the antibody has ADCC activity or CDC activity *in vitro* against the cell line, HepG2 or HUH-7 in the present of complement or peripheral blood mononuclear cells ..." See Office Action, page 3.

Applicants further submit that the present specification describes a process for obtaining these antibodies, e.g., on page 10, last line, to page 11, line 11, of the specification.

Accordingly, Applicants submit that the present specification does describe, e.g., that a plurality of antibodies (ch.M3C11 and ch.M1E07) with cytotoxic activity can be obtained in vitro in the present of complement or peripheral blood mononuclear cells as recited in the present claims. In particular, the specification describes that a person skilled in the art could select an antibody in vitro in the presence of complement or peripheral blood mononuclear cells as recited in the present claims.

Accordingly, Applicants respectfully assert that amended claim 9 complies with the written description requirement.

Applicants respectfully note that the present invention was achieved, e.g., based on the inventor's findings that the peptide fragment consisting of amino acid residues 375-580 of GPC3 as defined in SEQ ID NO: 4 remains anchored on the surface of a cell. Thus, Applicants submit that one can expect from the description of the specification, e.g., that an antibody recognizing an epitope within the amino acid residues 359-580 of GPC3 may exhibit the desired effect of the invention.

With regard to the Examiner's reference to *University of California v. Eli Lilly and Co.*, 119 F.3d 1559 (Fed. Cir. 1997) and *Enzo Biochem, Inc. v. Gen-Probe Inc.*, Applicants submit that unlike the invention of cDNA's, established examination practice for the inventions directed

to an antibody allows that the antibody be specified by its binding epitopes or its function, rather than by its structure.

For the foregoing reasons, withdrawal of the rejection is respectfully requested.

Conclusion

Reconsideration of the present application, as amended, is respectfully requested. If the Examiner has any questions or concerns regarding this response and amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number set forth below.

Respectfully submitted,
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